CLAIMS

WE CLAIM:

Sub A3 > 1. An injectable, non-tumorigenic mammalian retinal pigment epithelial cell line,

(a) wherein the cells of the cell line are selected from the group consisting of cells

(i) comprising a recombinant polynucleotide comprising an oncogene,

(ii) subjected to a spontaneous genetic modification leading to an extended life-span, and

(iii) comprising a recombinant polynucleotide comprising the human telomerase reverse transcriptase gene (hTRT) or a sequence able to activate the endogenous hTRT gene; and

(b) wherein the cells of the cell line can non-tumorigenically interact with retinal cells of a mammalian host.

2. The cell line of claim 1, wherein the oncogene is a heat-sensitive oncogene.

3. The cell line of claim 1, wherein the oncogene is a non-thermosensitive oncogene.

4. The cell line of claim 1, wherein the oncogene is a viral or cellular oncogene.

5. The cell line of claim 4, wherein the viral oncogenes are selected from the group consisting of SV-40 large T oncogene and the E1A early region of the adenovirus 2 genome.

6. The cell line of claim 4, wherein the cellular oncogenes are selected from the group consisting of c-myc and Ha-ras.

7. The cell line of claim 1, wherein the cells are rat cells.

8. The cell line of claim 7, wherein the cell line is IO/LD7, deposited under no. I-1694 on April 18, 1996 in the Collection Nationale de Cultures de Micro-organismes held by the Institut Pasteur, Paris France.

9. The cell line of claim 1, wherein the cells are human cells.

10. The cell line of claim 9, wherein the cells are of the hRPE cell line 7 or the hRPE cell line 116.

11. The cell line of claim 9, wherein the cells are of the ARPE-19 cell line.

12. The cell line of claim 1, wherein the oncogene, the human telomerase reverse transcriptase gene (hTRT), or the sequence able to activate the hTRT endogenous gene is located on an expression vector.

13. The cell line of claim 12, wherein the expression vector is selected from the group consisting of a plasmid and a viral vector.

14. The cell line of claim 13, wherein the viral vector is selected from the group consisting of LTR-based MFG, LXSN, LNSX, LNCX, lentivirus, adeno-associated virus.

15. The cell line of claim 12, wherein the expression vector is driven by a promoter selected from the group consisting of strong viral promoters, cell-specific promoters, housekeeping gene promoters, inducible promoters and hybrid promoters.

16. The cell line of claim 1, further

(c) wherein the cells of the cell line comprise an expression vector comprising a polynucleotide coding for a therapeutic polypeptide for treating primary or secondary ophthalmologic or neurological disorders;

(d) wherein the cells of the cell line can interact non-tumorigenically with retinal cells of the mammalian host to produce the polypeptide in the eye.

17. The cell line of claim 16, wherein the polypeptide is selected from the group of neurotrophins, interleukins, cytokines, anti-apoptotic, angiogenic, and anti-angiogenic factors, antigens , and immunomodulating peptides, immunoprotective peptides, protease inhibitors, prodrug converting enzymes or viral suicide genes, superoxide dismutase, or free radical scavengers.

18. The cell line of claim 16, wherein the polypeptide is selected from the group of BDNF, NT-4, CNTF, Axokine, FGF-2 (bFGF), IGF I, IGF II, TGFβ-II, Midkine, IL-1β, TNF, NGF, IL-2/3, ILF, IL-6, NTN, Neublastin, VEGF, GDNF, PDGF, LEDGF, PEDF.

19. A method for making a mammalian retinal pigment epithelial cell line, comprising:

(a) obtaining primary cultures of mammalian retinal pigment epithelial cells;

(b) introducing to the cells a gene selected from the group consisting of:

(i) an oncogene;

(ii) a human telomerase reverse transcriptase gene (hTRT); and

(iii) a sequence able to activate the hTRT endogenous gene

(c) selecting the recombinant cells;

(d) ensuring that the cells have an extended proliferation capacity; and

(e) selecting a passaged cell line that has at least one mammalian retinal pigment epithelial characteristic selected from the group consisting of pavement morphology, expression of RET-PE2, expression of cytokeratin, and combinations thereof.

20. A method of producing a polypeptide to treat primary or secondary ophthalmologic or neurological disorders, comprising incubating cells of a mammalian retinal pigment epithelial cell line in a biological compatible medium such that the cell line produce the polypeptide,

(a) wherein the cells of the cell line comprise a recombinant polynucleotide comprising a gene selcted from the group consisting of:

(i) an oncogene,

(ii) a recombinant polynucleotide comprising the human telomerase reverse transcriptase gene (hTRT), and

(iii) a sequence able to activate the hTRT endogenous gene; and

(b) wherein the cells of the cell line comprise an expression vector comprising a polynucleotide coding for a polypeptide for treating primary or secondary ophthalmologic or neurological disorders.

21. The method of claim 20, wherein the primary and secondary ophthalmologic or neurological disorders are selected from the group consisting of retinal degeneration, diabetic retinopathy, eye and retinal inflammation, eye and retinal primary and secondary tumors, neurological degenerative disorders, and neuronal degeneration.

22. The method of claim 20, wherein the cells are implanted in an eye of a mammalian host in need thereof.

23. The method of claim 22, wherein the cells are implanted in the subretinal space of the mammalian host.

24. A method of producing a therapeutic polypeptide to treat primary or secondary ophthalmologic or neurological disorders, comprising incubating cells of a mammalian retinal pigment epithelial cell line in a biological compatible medium such that the cell line produce the polypeptide,

(a) wherein the cells are subjected to a spontaneous genetic modification leading to an extended life-span; and

(b) wherein the cells of the cell line comprise an expression vector comprising a polynucleotide coding for a polypeptide for treating primary or secondary ophthalmologic or neurological disorders.

25. A method for treating primary or secondary ophthalmologic or neurological disorders, comprising non-tumorigenically grafting cells of a mammalian retinal pigment epithelial cell line into the eye of a mammalian host, wherein the cells of the cell line comprise a polynucleotide comprising a gene selected from the group consisting of:

(a) an oncogene;

(b) a recombinant polynucleotide comprising the human telomerase reverse transcriptase gene (hTRT); and

(c) a sequence able to activate the hTRT endogenous gene.

26. The methods of claim 25, wherein the cells comprise an expression vector comprising a therapeutic polynucleotide coding for a polypeptide to treat primary or secondary ophthalmologic or neurological disorders.

27. The method of claim 25, wherein the grafting of the cells is a surgical injection of the cells.

28. The methods of claim 25, wherein the cells are surgically injected into the subretinal space of the mammalian host.

29. The methods of claim 25, wherein the primary and secondary ophthalmologic or neurological disorders are selected from the group consisting of retinal degeneration, diabetic retinopathy, eye and retinal inflammation, eye and retinal primary and secondary tumors, neurological degenerative disorders, and neuronal degeneration.

30. A method for treating primary or secondary ophthalmologic or neurological disorders, comprising non-tumorigenically grafting cells of a mammalian retinal pigment epithelial cell line into the eye of a mammalian host, wherein the cells are subjected to a spontaneous genetic modification leading to an extended proliferation capacity.

31. An injectable, stable, non-tumorigenic mammalian retinal endothelial cell line

(a) wherein the cells of the cell line comprise a recombinant polynucleotide comprising a gene selected from the group consisting of:

(i) an oncogene;

(ii) a recombinant polynucleotide comprising the human telomerase reverse transcriptase gene (hTRT); and

(iii) a sequence able to activate the hTRT endogenous gene, and

(b) wherein the cells of the cell line can non-tumorigenically integrate into a retina of a mammalian host.

32. The cell line of claim 31, wherein the oncogene is a SV40 T-antigen oncogene.

33. The cell line of claim 31, wherein the cell line is IO/JG1, deposited under no. I-1695 on April 18, 1996 in the Collection Nationale de Cultures de Micro-organismes held by the Institut Pasteur, Paris France.

34. The cell line of claim 25, wherein the oncogene is located on an expression vector.

35. An injectable, stable, non-tumorigenic mammalian retinal endothelial cell line

(a) wherein the cells are subjected to a spontaneous genetic modification leading to an extended life-span.

(b) wherein the cells of the cell line can non-tumorigenically integrate into a retina of a mammalian host.

36. A method for making a rat retinal endothelial cell line, comprising:

(a) obtaining primary cultures of rat retinal endothelial cells;

(b) transfecting cells of the primary culture with an oncogene;

(c) selecting the transfected cells;

(d) cloning a cell line by limiting dilution of the selected transfected cells;

(e) passaging the cloned cell line for at least 30 passages; and

(f) selecting a passaged cell line that has a rat retinal endothelial characteristic selected from the group consisting of fusiform morphology, expression of RECA-1, expression of P-glycoprotein, expression of GLUT-1, expression of transferrin receptor, and combinations thereof.